Core-to-Core Program

THE UNIVERSITY OF TOKYO

東京大学ナノバイオ国際研究教育拠点セミナー #02

C2CNB Seminar Series

International Core Research Center for NanoBio , The University of Tokyo

The Human Platelet as an Innate Immunity Cell

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Date: Friday, February 14, 2014
Time: 15:00 - 16:00
Venue: #205 Seminar Room, Faculty of Engineering Bldg. 4, The University of Tokyo

Apart from the traditional view of platelets as mediators of hemostasis, evidence is emerging that indicates that platelet activation during thrombotic events is closely associated with activation of the complement and contact systems, leading to inflammation. The purpose of this lecture is to present data that support the concept that the human platelet is indeed an important actor within the innate immunity system.
By using experimental systems where platelets are activated by a synthetic thrombin receptor peptide, we have been able to dissect several mechanisms on the molecular level by which the activated platelet interact with key proteins within the complement and contact systems. Soluble mediators released from platelet granulae as well as the surface of the activated platelets are operative in these processes.

1) Extracellular phosphorylation of plasma proteins
Platelets contain high concentrations of ATP and Ca^{2+} in their dense granules, and when activated, they release these molecules along with Ser/Thr protein kinases. Both ATP and Ca^{2+} contribute to the extracellular phosphorylation of plasma proteins, including C3, fibrinogen, vitronectin and coagulation factor XI. The phosphorylation of Thr^{1009} of C3d influences C3 function by increasing the propensity of C3b to bind to activated surfaces. In addition, this phosphorylation attenuates the inactivation of C3b by inhibiting cleavage reactions that are mediated by factor I. Overall, C3 phosphorylation prolongs the period during which C3b is active, thereby amplifying complement activation.

2) Complement activation due to release of CS-A
Chondroitin sulfate A (CS-A) that is released from dense granulae during platelet activation is a potent mediator of the cross talk between platelets and the complement system. CS-A activates complement in the fluid phase, generating anaphylatoxins that mediate leukocyte activation.

3) Deposition of complement components on the surface of activated platelets.
No complement activation seems to occur on the activated platelet surface, but C3 in the form of $C3(H_2O)$ is bound to the surfaces of activated platelets, in addition to several other complement components. This is consistent with the strong expression of membrane-bound and high density of plasma derived complement regulators, partially CS-A-bound to the platelet surface. Platelet bound $C3(H_2O)$ acts as a ligand for leukocyte CR1 (CD35), potentially enabling platelet-leukocyte interaction.
In summary, in addition to its traditional role as an initiator of secondary hemostasis, platelets have been shown to act as a mediator and regulator of inflammation in thrombotic events.

Organizer: International Core Research Center for NanoBio, The University of Tokyo

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